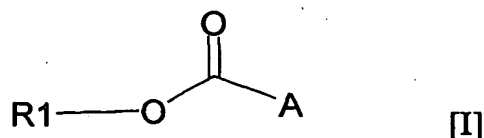


## CLAIMS:

1. Use of a compound of the general formula I:



- 5 or of a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>12</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, for the preparation of a pharmaceutical composition for treatment of inflammation.

10

2. The use according to claim 1 wherein R1 is a C<sub>12</sub>-C<sub>20</sub> alkyl or alkenyl.

3. The use according to claim 2 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

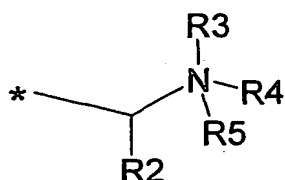
- 15 4. The use according to claim 3 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl.

5. The use according to claim 4 wherein R1 is cis-9-octadecenyl.

20

6. The use according to any one of claims 1 to 5 wherein in said compound of general formula I the residue A is selected from the group consisting of:

(i)

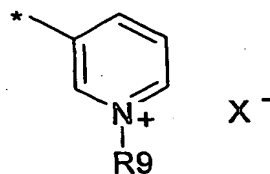


25

wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R6, R7 and R8 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

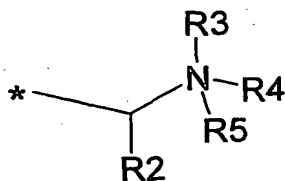
(ii) phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R6, R7 and R8 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

(iii)



wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X is absent.

7. The use according to claim 6 wherein the residue A is of the formula:



wherein R2 is H; a straight or branched C<sub>1</sub>-C<sub>6</sub> alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together

with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine.

5

8. The use according to claim 7 wherein R<sub>2</sub> is H or phenyl, R<sub>3</sub> is H, methyl or a pair of electrons, R<sub>4</sub> and R<sub>5</sub> are each H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sub>4</sub> and R<sub>5</sub> together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.

10

9. The use according to claim 8 wherein said compound is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;

(4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;

15

(4-Methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate;

4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;

$\alpha$ -Amino- $\alpha$ -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and

Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

20

10. The use according to claim 6 wherein the residue A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> is each independently H or 1 C<sub>1</sub>-C<sub>6</sub> alkyl.

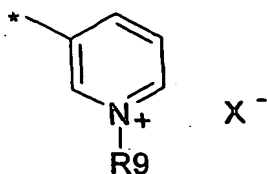
25

11. The use according to claim 10 wherein A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> is each methyl.

12. The use according to claim 11 wherein said compound is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

30

13. The use according to claim 6 wherein A is the group:



- wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl and X<sup>-</sup> is a counter ion,  
 5 or R9 is a pair of electrons and X<sup>-</sup> is absent.

14. The use according to claim 13 wherein R9 is a pair of electrons and X<sup>-</sup> is absent, or R9 is methyl or indolyethyl and X<sup>-</sup> is a counter ion selected from the group consisting of chloride, bromide, iodide and tosylate.

10

15. The use according to claim 14 wherein said compound is selected from the group consisting of:

Nicotinic acid octadec-(Z)-9-enyl ester;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;

15 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

1-[(2-(1H-indol-3-yl)-ethyl]-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

- 20 16. The use according to any one of claims 1 to 15 wherein said pharmaceutical composition is for treatment of immunologically-mediated inflammation.

17. The use according to claim 16 wherein said pharmaceutical composition is for the treatment of an immunologically-mediated chronic or acute inflammatory  
 25 disease, disorder or condition.

18. The use according to claim 17 wherein said pharmaceutical composition is for the treatment of an autoimmune disease, a severe allergy, asthma, or an inflammation associated with a disease, disorder or condition selected from graft rejection, a chronic degenerative disease such as Alzheimer's disease, neuroprotection, organ regeneration, chronic ulcers of the skin, or schizophrenia.

19. The use according to claim 18 wherein said autoimmune disease is multiple sclerosis or a human arthritic condition.

20. The use according to claim 19 wherein said human arthritic condition is rheumatoid arthritis, reactive arthritis with Reiter's syndrome, ankylosing spondylitis or other inflammation of the joints mediated by the immune system.

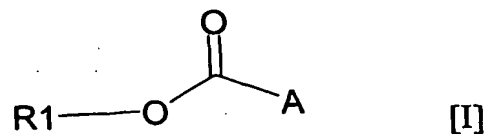
21. The use according to claim 17 wherein said immunologically-mediated inflammatory disease, disorder or condition is myasthenia gravis, Guillain-Barré syndrome, or other inflammatory disease of the nervous system; psoriasis, pemphigus vulgaris or other disease of the skin; systemic lupus erythematosus, glomerulonephritis or other disease affecting the kidneys; atherosclerosis or other inflammation of the blood vessels; autoimmune hepatitis, inflammatory bowel diseases, pancreatitis, or other disorder of the gastrointestinal system; type 1 diabetes mellitus, autoimmune thyroiditis, or other disease of the endocrine system.

22. The use according to claim 21 wherein said immunologically-mediated inflammatory disease or disorder is psoriasis.

23. The use according to any one of claims 1 to 22 wherein said pharmaceutical composition is for oral, topical, intradermal or parenteral administration.

24. The use according to claim 23 wherein said pharmaceutical composition is for subcutaneous, intravenous, or intramuscular administration.

25. A pharmaceutical composition for the treatment of inflammation comprising a pharmaceutically acceptable carrier and a compound of the general formula I:



5 or a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>12</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom.

10 26. The pharmaceutical composition according to claim 25 wherein R1 is a C<sub>12</sub>-C<sub>20</sub> alkyl or alkenyl.

27. The pharmaceutical composition according to claim 26 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

15

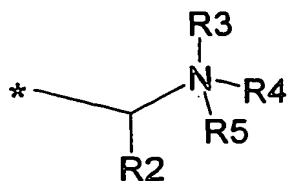
28. The pharmaceutical composition according to claim 27 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,

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29. The pharmaceutical composition according to claim 28 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

30. The pharmaceutical composition according to any one of claims 25 to 29 wherein in said compound of general formula I the residue A is selected from the group consisting of:

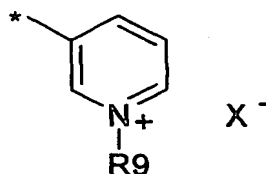
(i)



wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R6, R7 and R8 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

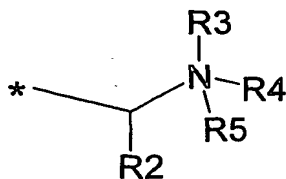
(ii) phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R6, R7 and R8 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

(iii)



wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X is absent.

31. The pharmaceutical composition according to claim 30 wherein the residue A has the formula:



wherein R<sub>2</sub> is H; a straight or branched C<sub>1</sub>-C<sub>6</sub> alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R<sub>3</sub> is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>4</sub> and R<sub>5</sub> each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sub>4</sub> and R<sub>5</sub> together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine.

32. The pharmaceutical composition according to claim 31 wherein R<sub>2</sub> is H or phenyl, R<sub>3</sub> is H or a pair of electrons, R<sub>4</sub> and R<sub>5</sub> are each H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sub>4</sub> and R<sub>5</sub> together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl.

33. The pharmaceutical composition according to claim 32 wherein said compound is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;  
(4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;  
(4-Methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate;  
4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;  
 $\alpha$ -Amino- $\alpha$ -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and  
Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

34. The pharmaceutical composition according to claim 30 wherein the residue A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

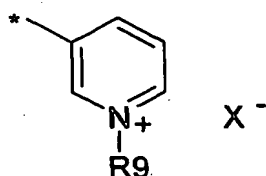
35. The pharmaceutical composition according to claim 34 wherein A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> each is methyl.



36. The pharmaceutical composition according to claim 35 wherein said compound is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

5

37. The pharmaceutical composition according to claim 30 wherein A is the group:



10 wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X<sup>-</sup> is absent.

38. The pharmaceutical composition according to claim 37 wherein R9 is a pair of electrons and X<sup>-</sup> is absent, or R9 is methyl or indolylethyl and X<sup>-</sup> is a counter ion  
15 selected from the group consisting of chloride, bromide, iodide and tosylate.

39. The pharmaceutical composition according to claim 38 wherein said compound is selected from the group consisting of:

20 Nicotinic acid octadec-(Z)-9-enyl ester;  
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;  
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;  
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and  
1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-enyloxycarbonyl-  
pyridinium bromide.

25

40. The pharmaceutical composition according to any one of claims 25 to 39, for treatment of immunologically-mediated inflammation.

41. The pharmaceutical composition according to claim 40 for the treatment of an immunologically-mediated chronic or acute inflammatory disease, disorder or condition.

5

42. The pharmaceutical composition according to claim 41 for the treatment of an autoimmune disease, a severe allergy, asthma, or an inflammation associated with a disease, disorder or condition selected from graft rejection, a chronic degenerative disease such as Alzheimer's disease, neuroprotection, organ  
10 regeneration, chronic ulcers of the skin, or schizophrenia.

43. The pharmaceutical composition according to claim 42 wherein said autoimmune disease is multiple sclerosis or a human arthritic condition.

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44. The pharmaceutical composition according to claim 43 wherein said human arthritic condition is rheumatoid arthritis, reactive arthritis with Reiter's syndrome, ankylosing spondylitis or other inflammation of the joints mediated by the immune system.

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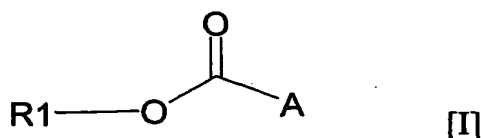
45. The pharmaceutical composition according to claim 40 wherein said immunologically-mediated inflammatory disease, disorder or condition is myasthenia gravis, Guillain-Barré syndrome, or other inflammatory disease of the nervous system; psoriasis, pemphigus vulgaris or other disease of the skin; systemic lupus erythematosus, glomerulonephritis or other disease affecting the kidneys;  
25 atherosclerosis or other inflammation of the blood vessels; autoimmune hepatitis, inflammatory bowel diseases, pancreatitis, or other disorder of the gastrointestinal system; type 1 diabetes mellitus, autoimmune thyroiditis, or other disease of the endocrine system.

46. The pharmaceutical composition according to claim 45 wherein said immunologically-mediated inflammatory disease or disorder is psoriasis.

47. The pharmaceutical composition according to any one of claims 25 to 46 for oral, topical, intradermal or parenteral administration.

48. The pharmaceutical composition according to claim 47 for subcutaneous, intravenous, or intramuscular administration.

49. A method for the treatment of inflammation which comprises administering to an individual in need thereof, an effective amount of a compound of the general formula I:



or of a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>12</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom.

50. The method according to claim 49 wherein R1 is a C<sub>12</sub>-C<sub>20</sub> alkyl or alkenyl.

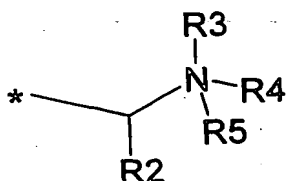
51. The method according to claim 50 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

52. The method according to claim 51 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,

53. The method according to claim 52 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

54. The method according to any one of claims 49 to 53 wherein in said compound of formula I the residue A is selected from the group consisting of:

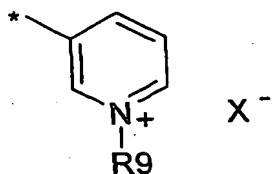
(i)



wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R6, R7 and R8 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

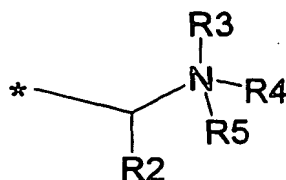
15 (ii) phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R6, R7 and R8 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

(iii)



20 wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X is absent.

55. The method according to claim 54 wherein the residue A is of the formula:



wherein R2 is H; a straight or branched C<sub>1</sub>-C<sub>6</sub> alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine.

56. The method according to claim 55 wherein R2 is H or phenyl, R3 is H or a pair of electrons, R4 and R5 are each H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl.

57. The method according to claim 56 wherein said compound is selected from the group consisting of:

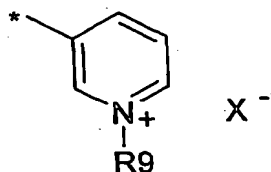
- N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;
- (4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;
- (4-Methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate;
- 4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;
- α-Amino-α-phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and
- Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

58. The method according to claim 54 wherein the residue A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

5 59. The method according to claim 58 wherein A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> is each methyl.

60. The method according to claim 59, wherein said compound is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-  
10 dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

61. The method according to claim 54 wherein A is the group:



15 wherein R<sub>9</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl and X<sup>-</sup> is a counter ion, or R<sub>9</sub> is a pair of electrons and X<sup>-</sup> is absent.

62. The method according to claim 61 wherein R<sub>9</sub> is a pair of electrons and X<sup>-</sup> is absent, or R<sub>9</sub> is methyl or indolyethyl and X<sup>-</sup> is a counter ion selected from the  
20 group consisting of chloride, bromide, iodide and tosylate.

63. The method according to claim 62 wherein said compound is selected from the group consisting of:

- Nicotinic acid octadec-(Z)-9-enyl ester;
- 25 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;
- 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;
- 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

64. The method according to any one of claims 49 to 63 for treatment of  
5 immunologically-mediated inflammation.

65. The method according to claim 64 for the treatment of an immunologically-mediated chronic or acute inflammatory disease, disorder or condition.

10 66. The method according to claim 65 for the treatment of an autoimmune disease, a severe allergy, asthma, or an inflammation associated with a disease, disorder or condition selected from graft rejection, a chronic degenerative disease such as Alzheimer's disease, neuroprotection, organ regeneration, chronic ulcers of the skin, or schizophrenia.

15

67. The method according to claim 66 wherein said autoimmune disease, disorder or condition is multiple sclerosis or a human arthritic condition.

20 68. The method according to claim 67 wherein said human arthritic condition is rheumatoid arthritis, reactive arthritis with Reiter's syndrome, ankylosing spondylitis or other inflammation of the joints mediated by the immune system.

25 69. The method according to claim 65 wherein said immunologically-mediated inflammatory disease, disorder or condition is myasthenia gravis, Guillain-Barré syndrome, or other inflammatory disease of the nervous system; psoriasis, pemphigus vulgaris or other diseases of the skin; systemic lupus erythematosus, glomerulonephritis or other disease affecting the kidneys; atherosclerosis or other inflammation of the blood vessels; autoimmune hepatitis, inflammatory bowel diseases, pancreatitis, or other disorder of the gastrointestinal system; type 1  
30 diabetes mellitus, autoimmune thyroiditis, or other disease of the endocrine system.

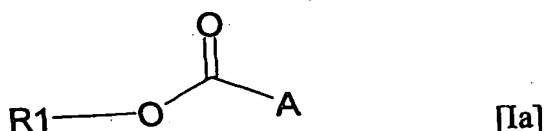
70. The method according to claim 69 wherein said immunologically-mediated inflammatory disease or disorder is psoriasis.

5 71. The method according to any one of claims 49 to 70 wherein said compound is administered by oral, topical, intradermal or parenteral route.

72. The method according to claim 71 wherein said compound is administered by subcutaneous, intravenous, or intramuscular route.

10

73. Use of an adjuvant of the general formula Ia:



or of a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>10</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic  
15 amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compounds wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one acyclic amino group or -CO-A is the residue of proline, for the preparation of a therapeutic preparation further comprising an antigen.

20

74. The use according to claim 73 wherein R1 is a C<sub>12</sub>-C<sub>20</sub> alkyl or alkenyl.

75. The use according to claim 74 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

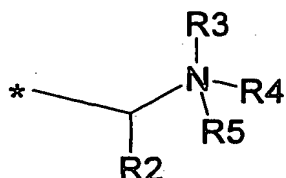
25 76. The use according to claim 75 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,



77. The use according to claim 76 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

78. The use according to any one of claims 73 to 77 wherein in said compound  
5 of formula I the residue A is selected from the group consisting of:

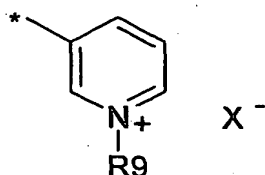
(i)



10 wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted  
15 by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl; and R6, R7 and R8 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

(ii) phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R6, R7 and R8 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

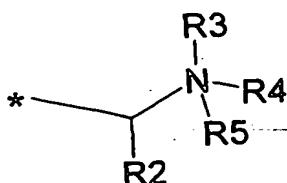
20 (iii)



wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X is absent.

25

79. The use according to claim 78 wherein the residue A has the formula:



5

wherein R2 is H; a straight or branched C<sub>1</sub>-C<sub>6</sub> alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine, provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl.

15

80. The use according to claim 79 wherein R2 is H or phenyl, R3 is H or a pair of electrons, R4 and R5 each is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl, provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl.

20

81. The use according to claim 80 wherein said compound is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;

25 (4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;

4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;

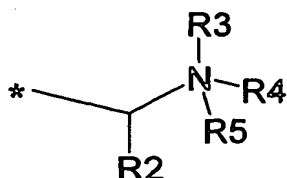
α-Amino-α-phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and

Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

82. The use according to claim 73 wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compound wherein -CO-A is the residue of proline.

83. The use according to claim 82 wherein the residue A has the formula:

(i)



wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R6, R7 and R8 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

84. The use according to claim 83 wherein R2 is H or phenyl, R3 is H or a pair of electrons, and R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl.

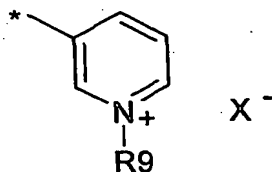
85. The use according to claim 84 wherein said compound is (4-methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate.

86. The use according to claim 78 wherein A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> is each independently H or 1 C<sub>1</sub>-C<sub>6</sub> alkyl.

5 87. The use according to claim 86 wherein A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> is each methyl.

88. The use according to claim 87 wherein said compound is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-  
10 dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

89. The use according to claim 78 wherein A is the group:



15 wherein R<sub>9</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl and X<sup>-</sup> is a counter ion, or R<sub>9</sub> is a pair of electrons and X<sup>-</sup> is absent.

90. The use according to claim 89 wherein R<sub>9</sub> is a pair of electrons and X<sup>-</sup> is absent, or R<sub>9</sub> is methyl or indolyethyl and X<sup>-</sup> is a counter ion selected from the  
20 group consisting of chloride, bromide, iodide and tosylate.

91. The use according to claim 90 wherein said compound is selected from the group consisting of:

Nicotinic acid octadec-(Z)-9-enyl ester;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;

25 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

92. Use of an adjuvant according to any one of claims 73 to 91 wherein said  
5 adjuvant is administered with an antigen that raises a humoral response.

93. Use of an adjuvant according to any one of claims 73 to 91 wherein said  
adjuvant is administered with an antigen that raises a cellular response.

10 94. Use according to claim 93 for treatment of a T-cell mediated disease,  
disorder or condition, wherein said antigen is an antigen recognized by  
inflammatory T cells associated with the pathogenesis of said T-cell mediated  
disease, disorder or condition.

15 95. Use according to claim 93 wherein said therapeutic preparation causes  
shifting of an individual's T-cell cytokine response from  $T_H1$  to  $T_H2$ .

96. Use according to claim 95 wherein said therapeutic preparation causes a  
decrease in IL-2 or IFN- $\gamma$  T-cell cytokine response and an increase in IL-4 or IL-10  
20 T-cell cytokine response.

97. Use according to any one of claims 94 to 96 wherein said T-cell mediated  
disease, disorder or condition is an autoimmune disease and said antigen is a peptide.

25 98. Use according to claim 97, wherein said autoimmune disease is an organ-  
specific autoimmune disease.

99. Use according to claim 98 wherein said organ-specific autoimmune disease is  
type I diabetes mellitus, multiple sclerosis, rheumatoid arthritis or autoimmune  
30 thyroiditis.

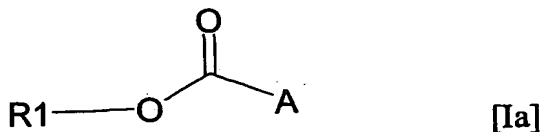
100. Use according to claim 99 for the treatment of multiple sclerosis wherein said antigen is a peptide derived from the sequence of myelin basic protein (MBP) or an analogue thereof that is recognized by T-cells involved in the pathogenesis of multiple sclerosis.

101. Use according to claim 99 for the treatment of multiple sclerosis wherein said antigen is a copolymer recognized by T-cells involved in the pathogenesis of multiple sclerosis.

102. Use according to claim 101 wherein said antigen is glatiramer acetate.

103. Use according to any one of claims 73 to 91 wherein said therapeutic preparation comprises said adjuvant and an antigen useful for treatment of an autoimmune disease, a neurodegenerative disease such as Alzheimer's disease or Parkinson disease, a cancer such as melanoma, or an infectious disease such as a bacterial or viral infection.

104. A therapeutic preparation comprising an antigen and an adjuvant of the general formula Ia:



or a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>10</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compounds wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one acyclic amino group or -CO-A is the residue of proline.

105. The therapeutic preparation according to claim 104 wherein R1 is a C<sub>12</sub>-C<sub>20</sub> alkyl or alkenyl.

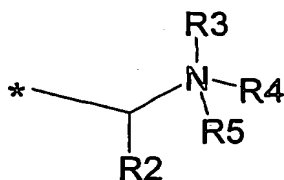
106. The therapeutic preparation according to claim 105 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

107. The therapeutic preparation according to claim 106 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,

108. The therapeutic preparation according to claim 107 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

109. The therapeutic preparation according to any one of claims 104 to 108 wherein in said adjuvant of formula Ia the residue A is selected from the group consisting of:

(i)

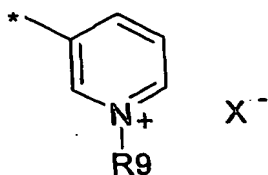


wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl,

provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl; and R6, R7 and R8 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl;

(ii) phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R6, R7 and R8 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

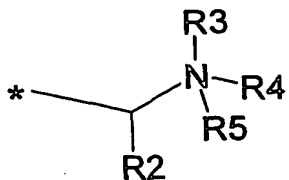
5 (iii)



wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X is absent.

10

110. The therapeutic preparation according to claim 109 wherein the residue A has the formula:



15

wherein R2 is H; a straight or branched C<sub>1</sub>-C<sub>6</sub> alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, said ring being selected from the group consisting of pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine, provided

20

25 that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl.



111. The therapeutic preparation according to claim 110 wherein R2 is H or phenyl, R3 is H or a pair of electrons, R4 and R5 is each H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl, provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl.

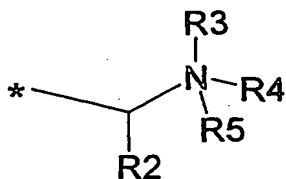
112. The therapeutic preparation according to claim 111 wherein said adjuvant is selected from the group consisting of:

N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;  
 (4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;  
 4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;  
 $\alpha$ -Amino- $\alpha$ -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and  
 Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

113. The therapeutic preparation according to claim 104 wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compound wherein -CO-A is the residue of proline.

114. The therapeutic preparation according to claim 113 wherein the residue A has the formula:

(i)



wherein R<sub>2</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R<sub>3</sub> is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>4</sub> and R<sub>5</sub> together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

115. The therapeutic preparation according to claim 114 wherein R<sub>2</sub> is H or phenyl, R<sub>3</sub> is H or a pair of electrons, and R<sub>4</sub> and R<sub>5</sub> together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.

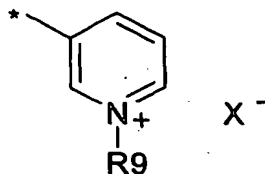
116. The therapeutic preparation according to claim 115 wherein said adjuvant is (4-methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate.

117. The therapeutic preparation according to claim 109 wherein A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

118. The therapeutic preparation according to claim 117 wherein A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> is each methyl.

119. The therapeutic preparation according to claim 118 wherein said adjuvant is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

120. The therapeutic preparation according to claim 109 wherein A is the group:



wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl and X<sup>-</sup> is a counter ion, or R9 is a pair of electrons and X<sup>-</sup> is absent.

5 121. The therapeutic preparation according to claim 120 wherein R9 is a pair of electrons and X<sup>-</sup> is absent, or R9 is methyl or indolyethyl and X<sup>-</sup> is a counter ion selected from the group consisting of chloride, bromide, iodide and tosylate.

122. The therapeutic preparation according to claim 121 wherein said adjuvant is  
10 selected from the group consisting of:

Nicotinic acid octadec-(Z)-9-enyl ester;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;

1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

15 1-[(2-(1H-indol-3-yl)-ethyl]-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

123. A therapeutic preparation according to any one of claims 104 to 122 comprising said adjuvant and an antigen that raises a humoral response.

20

124. A therapeutic preparation according to any one of claims 104 to 122 comprising said adjuvant and an antigen that raises a cellular response.

125. The therapeutic preparation according to claim 124 for treatment of a T-cell  
25 mediated disease, disorder or condition, wherein said antigen is an antigen recognized by inflammatory T cells associated with the pathogenesis of said T-cell mediated disease, disorder or condition.

126. The therapeutic preparation according to claim 125 wherein said therapeutic preparation causes shifting of an individual's T-cell cytokine response from  $T_H1$  to  $T_H2$ .

5

127. The therapeutic preparation according to claim 126 wherein said therapeutic preparation causes a decrease in IL-2 or IFN- $\gamma$  T-cell cytokine response and an increase in IL-4 or IL-10 T-cell cytokine response.

10 128. The therapeutic preparation according to any one of claims 125 to 127 wherein said T-cell mediated disease is an autoimmune disease and said antigen is a peptide.

129. The therapeutic preparation according to claim 128, wherein said  
15 autoimmune disease is an organ-specific autoimmune disease.

130. The therapeutic preparation according to claim 129 wherein said organ-specific autoimmune disease is type I diabetes mellitus, multiple sclerosis, rheumatoid arthritis or autoimmune thyroiditis.

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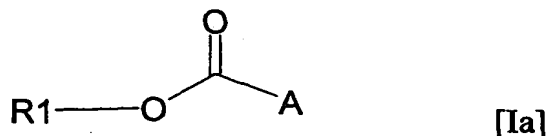
131. The therapeutic preparation according to claim 130 for the treatment of multiple sclerosis wherein said antigen is a peptide derived from the sequence of myelin basic protein (MBP) or an analogue thereof that is recognized by T-cells involved in the pathogenesis of multiple sclerosis.

25 132. The therapeutic preparation according to claim 130 for the treatment of multiple sclerosis wherein said antigen is a copolymer recognized by T-cells involved in the pathogenesis of multiple sclerosis.

133. The therapeutic preparation according to claim 132 wherein said antigen is glatiramer acetate.

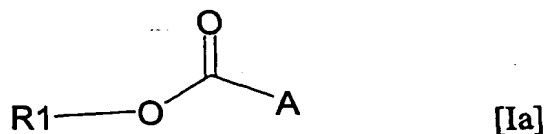
134. The therapeutic preparation according to any one of claims 104 to 122 wherein said antigen is useful for treatment of an autoimmune disease, a neurodegenerative disease such as Alzheimer's disease or Parkinson disease, a cancer such as melanoma, or an infectious disease such as a bacterial or viral infection.

135. A method of treating a T-cell mediated disease, disorder or condition, which comprises administering to an individual in need an effective amount of a therapeutic preparation comprising an antigen recognized by inflammatory T cells associated with the pathogenesis of said T-cell mediated disease, disorder or condition, and an adjuvant of the general formula Ia:



or a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>10</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compounds wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one acyclic amino group or -CO-A is the residue of proline.

136. A method of causing a shifting of T-cell cytokine response from T<sub>H</sub>1 to T<sub>H</sub>2 in an individual suffering from a T-cell mediated disease, disorder or condition, which comprises administering to said individual in need an effective amount of a therapeutic preparation comprising an antigen recognized by inflammatory T cells associated with the pathogenesis of said T-cell mediated disease, disorder or condition and an adjuvant of the general formula Ia:



or a pharmaceutically acceptable salt thereof, wherein R1 is C<sub>10</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl, and A is a residue containing at least one acyclic or cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compounds wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one acyclic amino group or -CO-A is the residue of proline.

137. The method according to claim 136 wherein said therapeutic preparation causes a decrease in IL-2 or IFN- $\gamma$  T-cell cytokine response and an increase in IL-4 or IL-10 T-cell cytokine response.

138. The method according to claim 135 or 136 wherein R1 is a C<sub>12</sub>-C<sub>20</sub> alkyl or alkenyl.

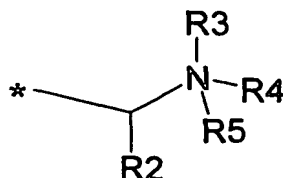
139. The method according to claim 138 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

140. The method according to claim 139 wherein R1 is hexadecyl, octadecyl, hexadecenyl, octadecenyl, cis-9-octadecenyl, trans-9-octadecenyl, cis-9,12-octadecadienyl, cis-6,9,12-octadecatrienyl, or cis-9,12,15-octadecatrienyl,

141. The method according to claim 140 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

142. The method according to any one of claims 135 to 141 wherein in said compound of formula Ia the residue A is selected from the group consisting of:

(i)

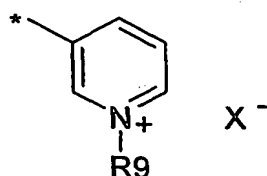


wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may  
 5 be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or  
 CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 is each  
 independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to  
 which they are attached form a 5-7 membered saturated ring optionally interrupted  
 by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl,  
 10 provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl; and R6, R7  
 and R8 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl;

(ii) phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R6, R7 and R8  
 each is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

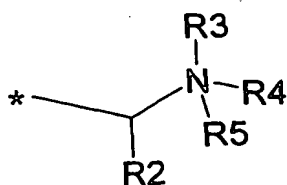
(iii)

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wherein R9 is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, and X<sup>-</sup> is a counter ion,  
 or R9 is a pair of electrons and X is absent.

20 143. The method according to claim 142 wherein the residue A has the formula:



wherein R2 is H; a straight or branched C<sub>1</sub>-C<sub>6</sub> alkyl selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, pentyl and  
 5 hexyl; phenyl, benzyl or p-hydroxybenzyl; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl, said ring being selected from the group consisting of  
 10 pyrrolidine, piperidine, morpholine, piperazine, and 4-methylpiperazine, provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl.

144. The method according to claim 143 wherein R2 is H or phenyl, R3 is H or a pair of electrons, R4 and R5 is each H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with  
 15 the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 1 or 4 by methyl, provided that R4 and R5 are not H or C<sub>1</sub>-C<sub>6</sub> alkyl when R1 is octadecyl.

145. The method according to claim 144 wherein said adjuvant is selected from  
 20 the group consisting of:

- N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;
- (4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;
- 4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;
- α-Amino-α-phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt; and
- 25 Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.

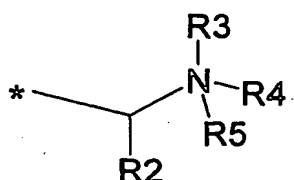


146. The method according to claim 135 or 136 wherein R1 is C<sub>18</sub> alkyl and A is a residue containing at least one cyclic amino group and/or at least one heteroaromatic ring containing a tertiary or quaternary nitrogen atom, but excluding the compound wherein -CO-A is the residue of proline.

5

147. The method according to claim 146 wherein the residue A has the formula:

(i)



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wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R6, R7 and R8 is each independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

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148. The method according to claim 147 wherein R2 is H or phenyl, R3 is H or a pair of electrons, and R4 and R5 together with the N atom to which they are attached form a morpholine ring or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.

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149. The method according to claim 148 wherein said adjuvant is (4-methyl-25 piperazin-1-yl)-acetic acid octadecyl ester tartrate.

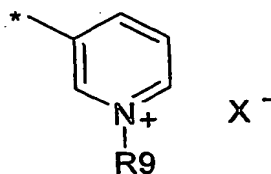
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150. The method according to claim 142 wherein A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> is each independently H or 1 C<sub>1</sub>-C<sub>6</sub> alkyl.

5 151. The method according to claim 150 wherein A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> is each methyl.

152. The method according to claim 151 wherein said adjuvant is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-  
10 dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

153. The method according to claim 142 wherein A is the group:



15 wherein R<sub>9</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>4</sub>)alkyl and X<sup>-</sup> is a counter ion, or R<sub>9</sub> is a pair of electrons and X<sup>-</sup> is absent.

154. The method according to claim 153 wherein R<sub>9</sub> is a pair of electrons and X<sup>-</sup> is absent, or R<sub>9</sub> is methyl or indolylethyl and X<sup>-</sup> is a counter ion selected from the  
20 group consisting of chloride, bromide, iodide and tosylate.

155. The method according to claim 154 wherein said adjuvant is selected from the group consisting of:

- Nicotinic acid octadec-(Z)-9-enyl ester;
- 25 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;
- 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;
- 1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and

1-[(2-(1H-indol-3-yl)-ethyl)-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

156. The method according to any one of claims 135 to 155 wherein said antigen  
5 raises a humoral response in said individual.

157. The method according to any one of claims 135 to 155 wherein said antigen  
raises a cellular response in said individual.

10 158. The method according to any one of claims 135 to 155 wherein said T-cell  
mediated disease is an autoimmune disease and said antigen is a peptide.

159. The method according to claim 158, wherein said autoimmune disease is an  
organ-specific autoimmune disease.

15

160. The method according to claim 159 wherein said organ-specific autoimmune  
disease is type I diabetes mellitus, multiple sclerosis, rheumatoid arthritis or  
autoimmune thyroiditis.

20 161. The method according to claim 160 for the treatment of multiple sclerosis  
wherein said antigen is a peptide derived from the sequence of myelin basic protein  
(MBP) or an analogue thereof that is recognized by T-cells involved in the  
pathogenesis of multiple sclerosis.

25 162. The method according to claim 160 for the treatment of multiple sclerosis  
wherein said antigen is a copolymer recognized by T-cells involved in the  
pathogenesis of multiple sclerosis.

163. The method according to claim 162 wherein said antigen is glatiramer  
acetate.

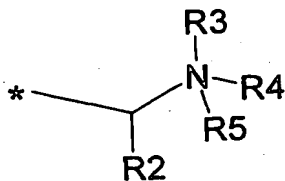
164. The method according to claim 135 or 136 wherein said therapeutic preparation comprises said adjuvant and an antigen useful for treatment of an autoimmune disease, a neurodegenerative disease such as Alzheimer's disease or Parkinson disease, a cancer such as melanoma, or an infectious disease such as a bacterial or viral infection.

165. A compound of the general formula:



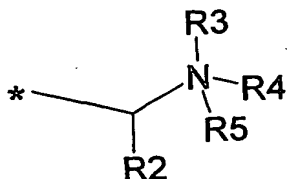
10 wherein

(i) R1 is C<sub>20</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl and A is a residue of the formula:



15 wherein R2 is H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, or aralkyl, wherein any aryl moiety may be unsubstituted or substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R3 is H, a pair of electrons, or C<sub>1</sub>-C<sub>6</sub> alkyl; R4 and R5 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and  
20 R6, R7 and R8 each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl; or

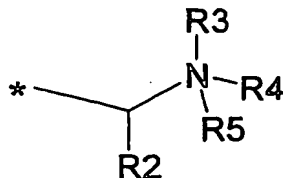
(ii) R1 is C<sub>18</sub> alkyl and A is a residue of the formula:



wherein R2 is H; R3 is a pair of electrons; and R4 and R5 together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring

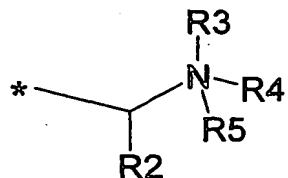
optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; or

(iii) R<sub>1</sub> is C<sub>12</sub>-C<sub>16</sub> alkyl and A is a residue of the formula:



5            wherein R<sub>2</sub> is unsubstituted aryl, or aryl or aralkyl wherein the aryl moiety is substituted by nitro, cyano, halo, hydroxy, NR<sub>6</sub>R<sub>7</sub>, or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>; R<sub>3</sub> is H, a pair of electrons, or C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>4</sub> and R<sub>5</sub> each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sub>4</sub> and R<sub>5</sub> together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl; or

(iv) R<sub>1</sub> is C<sub>10</sub> alkyl and A is a residue of the formula:

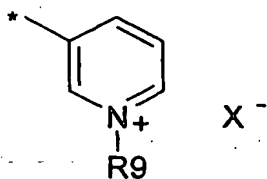


15            wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>3</sub> is H, a pair of electrons, or C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>4</sub> and R<sub>5</sub> each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sub>4</sub> and R<sub>5</sub> together with the nitrogen atom to which they are attached form a 5-7 membered saturated ring optionally interrupted by an oxygen atom or by a nitrogen atom optionally substituted by C<sub>1</sub>-C<sub>6</sub> alkyl; and R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl; or

20            (v) R<sub>1</sub> is C<sub>10</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl and A is phenyl substituted by NR<sub>6</sub>R<sub>7</sub> or CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> each independently is H or C<sub>1</sub>-C<sub>6</sub> alkyl, but excluding the compounds wherein R<sub>1</sub> is C<sub>10</sub>-C<sub>16</sub> alkyl and A is phenyl substituted by -CH<sub>2</sub>-NH<sub>2</sub>; or

(vi) R<sub>1</sub> is C<sub>10</sub>-C<sub>24</sub> alkyl or C<sub>10</sub>-C<sub>24</sub> alkenyl and A is a group of the formula:

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wherein R9 is C<sub>1</sub>-C<sub>6</sub> alkyl or indolyl(C<sub>1</sub>-C<sub>6</sub>)alkyl and X<sup>-</sup> is a counter ion; and pharmaceutically acceptable salts thereof.

- 5 166. A compound according to claim 165(i), (v) or (vi) wherein R1 is a C<sub>12</sub>-C<sub>18</sub> alkenyl.
167. A compound according to claim 166 wherein R1 is a C<sub>16</sub>-C<sub>18</sub> alkenyl.
- 10 168. A compound according to claim 167 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.
169. A compound according to claim 168 wherein R2 is H or phenyl, R3 is H or a pair of electrons, and R4 and R5 are methyl or together with the N atom to which they are attached form a morpholino or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.
- 15 170. A compound according to claim 169 selected from the group consisting of:  
N,N-Dimethylamino-acetic acid octadec-(Z)-9-enyl ester;  
20 (4-Methyl-piperazin-1-yl)-acetic acid octadec-(Z)-9-enyl ester tartrate;  
4-Methyl-4-octadec-(Z)-9-enyloxycarbonylmethyl-morpholin-4-ium chloride;  
Piperazin-1-yl-acetic acid octadec-(Z)-9-enyl ester bitartrate.
171. A compound according to claim 165(ii) wherein R1 is octadecyl and R4 and R5 together with the N atom to which they are attached form a morpholino or a piperazine ring optionally substituted at the nitrogen atom at position 4 by methyl.
- 25

172. A compound according to claim 171 which is (4-methyl-piperazin-1-yl)-acetic acid octadecyl ester tartrate.

173. A compound according to claim 165(vi) wherein R1 is C<sub>12</sub>-C<sub>20</sub> alkyl or C<sub>12</sub>-C<sub>20</sub> alkenyl and A is phenyl substituted by CR<sub>8</sub>R<sub>8</sub>NR<sub>6</sub>R<sub>7</sub>, wherein R<sub>8</sub> is H and R<sub>6</sub> and R<sub>7</sub> is each H or C<sub>1</sub>-C<sub>6</sub> alkyl.

174. A compound according to claim 173 wherein R1 is C<sub>16</sub>-C<sub>18</sub> alkenyl.

175. A compound according to claim 174 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

176. A compound according to claim 175 which is 4-dimethylaminomethyl-benzoic acid octadec-(Z)-9-enyl ester HCl or 4-dimethylaminomethyl-benzoic acid octadec-(E)-9-enyl ester HCl.

177. A compound according to claim 165(vi) wherein R1 is C<sub>12</sub>-C<sub>20</sub> alkyl or C<sub>12</sub>-C<sub>20</sub> alkenyl.

178. A compound according to claim 177 wherein R1 is C<sub>16</sub>-C<sub>18</sub> alkyl or alkenyl.

179. A compound according to claim 178 wherein R1 is cis-9-octadecenyl or trans-9-octadecenyl.

180. A compound according to claim 179 selected from the group consisting of:  
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium iodide;  
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium chloride;  
1-Methyl-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium tosylate; and  
1-[(2-(1H-indol-3-yl)-ethyl]-3-octadec-(Z)-9-enyloxycarbonyl-pyridinium bromide.

181. A compound according to claim 165(i) wherein R1 is cis-9-octadecenyl, R2 is phenyl, R3 is a pair of electrons and R4 and R is each H.

5 182. The compound of claim 181 which is  $\alpha$ -amino- $\alpha$ -phenyl-acetic acid octadec-(Z)-9-enyl ester HCl salt.

183. A pharmaceutical composition comprising a compound according to any one of claims 165 to 182 or a pharmaceutically acceptable salt thereof, and a  
10 pharmaceutically acceptable carrier.

184. A pharmaceutical composition according to claim 183 for the treatment of inflammation.

15 185. A therapeutic composition comprising an antigen and an adjuvant according to any one of claims 165 to 182.

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